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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,992	10/13/2000	Craig C. Mello	07917-105001 / UMMC 00-04	1020

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EXAMINER

STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 11/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/689,992

Applicant(s)

MELLO ET AL.

Examiner

Teresa E Strzelecka

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 17-34 is/are pending in the application.
- 4a) Of the above claim(s) 1-13 and 23-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14 and 17-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 August 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. This Office action is in response to an amendment filed on August 12, 2002.
2. Claims 1-16 were pending in the application, of which claims 1-13 were withdrawn from consideration. Claims 15 and 16 were cancelled, claim 14 was amended. Claims 17-34 were added. Of the newly added claims, claims 17-22 depend on claim 14, claim 23 is an independent claim and claims 24-34 depend on claim 23.
3. Newly submitted claims 23-34 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 23 is drawn to a method of inhibiting the activity of a gene in a cell, the method comprising:
 - introducing the RNAi pathway component into the cell, and
 - introducing a double-stranded RNA into the cell, wherein the dsRNA is targeted to the gene.Therefore, the new claim 23 is not drawn to a species of claim 14, and would have been restricted into a separate group if it was presented in the original set of claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 23-34 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 1-13 are also withdrawn from consideration.
4. Claims 14 and 17-22 will be examined. This Office action is made non-final because of new grounds of rejections presented below.

Drawings

5. The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on August 12, 2002 have been disapproved because they introduce new matter into the drawings. 37 CFR 1.121(a)(6) states that no amendment may introduce new matter into the disclosure of an application. The original disclosure does not support the showing of SEQ ID NO: 13 for RDE-1 sequence in Figure 4B.

Specification

6. The amendment filed on August 12, 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: new sequence listing was submitted, which "... corrects inadvertent errors that were made in the originally submitted sequence listing...". Applicants do not explain what the errors were and why the sequence listing had to be corrected. There is no evidence that a new CRF of the sequence listing was submitted with the paper copy.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 14 and 17-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting an activity of a gene by introducing an RNAi agent into the cell of *C. elegans*, does not reasonably provide enablement for inhibiting an activity of a gene by introducing an RNAi agent into the cell of any other organism. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants define an RNAi agent as a double-stranded RNA (dsRNA) molecule which has been treated with those components of the RNAi pathway that are recognized to confer RNAi activity on the dsRNA. In the case of *C. elegans*, these components were determined to be RDE-1 and RDE-4 proteins (page 6, lines 14-17). An RNAi pathway component is defined as a protein or nucleic acid that is involved in promoting dsRNA-mediated interference (page 5, lines 9-12). In *C. elegans*, the components of the RNAi pathway were determined to be genes *rde-1*, *rde-2*, *rde-3*, *rde-4*, *rde-5*, *mut-2* and *mut-7* (page 2, lines 11-31).

Gene silencing using dsRNA has been observed in several organisms, such as fruit fly *Drosophila melanogaster* (Misquitta et al., PNAS USA, vol. 96, pp. 1451-6, February 1999; Kennerdell et al., Cell, vol. 95, pp. 1017-26, December 1998; both cited in the IDS), metazoans (Sanchez Alvarado et al., PNAS USA, vol. 96, pp. 5049-54, April 1999; cited in the IDS), *Trypanosoma brucei* (Ngo et al., PNAS USA, vol. 95, pp. 14687-92, December 1998; cited in the IDS) and plants (Waterhouse et al., PNAS USA, vol. 95, pp. 13959-64, November 1998; cited in the IDS). However, no specific genes or gene products were identified which could be classified as "components of the RNAi pathway" in these organisms. In addition, there is an added complication arising in mammalian cells, as described by Montgomery et al. (Trends in Genetics, Vol. 14, pp. 255-8, July 1998; cited in the IDS). These cells exhibit a global antiviral response to dsRNA, in which the PKR protein kinase recognizes dsRNA and cause a non-specific response which results in general transcriptional arrest. "Any gene-specific interference by dsRNA in PKR-proficient mammalian cells would be dependent on a transient lapse in the PKR response, or on a controlled level of dsRNA that was incapable of activating PKR." (page 258, fourth paragraph).

Therefore, to create effective RNAi agents in organisms other than *C. elegans* one would have to determine which genes belong to the pathway in each of the organisms, then evaluate which ones are essential for promoting dsRNA-mediated interference, and, in mammalian cells, determine how to overcome the non-specific PKR-mediated response.

Due to the large quantity of experimentation necessary to determine all the components of the RNAi pathways in all organisms, the lack of direction/guidance presented in the specification regarding determination of all the components of the RNAi pathways in all organisms, the absence of working examples directed to determination of all the components of the RNAi pathways in all organisms, the complex nature of the invention, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

9. No references were found teaching or suggesting claims 14 and 17-22, but they are rejected for other reasons.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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November 13, 2002

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Kenneth R. Horlick
KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

11/13/02